Remarks

I. Status of the Claims

Upon entry of the foregoing amendment, claims 89-154 are pending in the application, with claims 89, 91, 98-103, 105, 106, 108, 109, 117, 118 and 122-124 being the independent claims. New claims 127-154 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider the sole outstanding rejection and that it be withdrawn.

II. Support for New Claims

Support for new claims 127, 128, 131, 132, 135, 136, 139, 140, 143, 144, 147, 148, 151 and 152 can be found, for example, in the specification at page 23, lines 14-16.

Support for new claims 129, 130, 133, 134, 137, 138, 141, 142, 145, 146, 149, 150, 153 and 154 can be found, for example, in the specification at page 23, lines 27-29.

III. Improper Advisory Action

Applicants note that the Advisory Action dated June 24, 2002 (Paper No. 24) was improperly issued by the Examiner. Applicants' previous Reply was a Reply Under 37 C.F.R. § 1.111 which was submitted on June 12, 2002 in response to the *non-final* Office Action dated March 12, 2002 (Paper No. 19). Under 37 C.F.R. § 1.112, after reply by an Applicant to a non-final action, the application is to be reconsidered and again examined.

An Advisory Action is proper only upon receipt of a Reply to a *final* Office Action. *See* MPEP § 714.13. Thus, it was improper for the Examiner to issue the Advisory Action rather than a further Office Action.

Applicants' undersigned representative contacted the Examiner by telephone on July 2, 2002 and informed the Examiner of the impropriety of the June 24, 2002 Advisory Action. On September 4, 2002, Applicants' undersigned representative again contacted the Examiner by telephone and indicated that the present Supplemental Reply would be filed to address certain issues raised by the Examiner in the June 24, 2002 Advisory Action. Applicants believe that this Supplemental Reply, along with the Declarations Under 37 C.F.R. § 1.132, submitted herewith, will assist in overcoming the outstanding rejection and therefore will advance the prosecution of this application.

IV. Rejection Under 35 U.S.C. § 112, First Paragraph

In the Advisory Action, the Examiner indicated that he would maintain the rejection of claims 89-126 under 35 U.S.C. § 112, first paragraph. Applicants respectfully traverse this rejection.

The Examiner has maintained the position that the term "embryonic stem cells," as used in the present claims, means *totipotent* embryonic stem cells. *See* Paper No. 24, page 2. Applicants respectfully disagree with this interpretation of the claim language. As noted previously, the term "embryonic stem cell" is not limited to totipotent embryonic stem cells. *See* Reply filed June 12, 2002, pages 4-5. First, there is nothing in the specification that necessitates that the cells be totipotent. The Examiner has cited a portion of the *Background of the Invention* section of the present specification to support the position that the term

"embryonic stem cells" means totipotent embryonic stem cells. *See* Paper No. 24, page 2 (citing the specification at page 1, lines 8-9). The cited text, however, merely provides technical background information regarding the field of the invention in general. This background section would *not* be relied upon by a skilled artisan to determine the metes and bounds of the expression "embryonic stem cell." Rather, the skilled artisan would look to the *Detailed Description of the Invention* section wherein "embryonic stem cell" is explicitly defined as "a cell which can give rise to *many differentiated cell types* in an embryo or an adult, including the germ cells (sperm and eggs)." *See* specification at page 14, lines 1-3 (emphasis added). Moreover, consistent with the definition put forth in the specification, it is understood in the art that the term "embryonic stem cell" is not limited to totipotent embryonic stem cells but also includes *pluripotent* embryonic stem cells. *See, e.g.*, Du, F. *et al.*, *J. Reproduct. Fertil. 104*:219-223 (1995) (copy submitted as "Attachment 3" with the Reply filed on August 9, 2000) (*see* especially the first sentence of the *Introduction*, referring to "*Pluripotent* embryonic stem (ES) cells."); *see also* specification at page 14, lines 1-4.

The Examiner has also maintained the position that there is no indication that conditions that have been shown to be useful for culturing mouse embryonic stem cells would also be effective for culturing embryonic stem cells from other animals. *See* Paper No. 19, pages 5-6. In the Reply filed on June 12, 2002, Applicants noted that there are several examples in the scientific literature showing that media and conditions that have been shown to be effective for mouse ES cells are also suitable for culturing and maintaining human ES cells and ES cells from other primates. *See* June 12, 2002 Reply, pages 10-12.

To support the assertion that conditions that have been shown to be useful for culturing mouse embryonic stem cells are also effective for culturing embryonic stem cells from other animals, Applicants submitted eight references, designated Exhibits A-H. Each of these references show the effective use of media comprising serum replacement to culture human and other primate embryonic stem cells. Exhibits A, C, D, F and H, in particular, describe the use of the product KNOCKOUT™ SR. Since KNOCKOUT™ SR is a serum replacer that has been demonstrated to be effective in culturing mouse embryonic stem cells, these five references directly support the assertion that conditions that have been shown to be effective for culturing mouse embryonic stem cells are also effective for culturing embryonic stem cells from other animals.

In response to this evidence, the Examiner stated:

> A review of the references submitted with the instant amendment some of the references teach that ES cells can be cultured in the absence of serum (though some methods use serum). However, an apparent requirement is the serum supplement, KnockOut SR. The specific nature and composition of the serum supplement is not disclosed in any of the references so it is difficult to assess whether the examples provided by these references are supported by the present disclosure.

See Advisory Action, page 4.

Applicants emphasize that the cited references were submitted primarily to illustrate that conditions that have been shown to be useful for culturing mouse embryonic stem cells are also effective for culturing embryonic stem cells from other animals. This contradicts the Examiner's view that "conditions for one ES cell may not be effective for the other ES cells. . ." *See* Paper No. 19, page 6. The evidence presented in the submitted references supports Applicants' assertion that a skilled artisan could look to methods and compositions

that have been used to successfully culture embryonic stem cells (*e.g.*, mouse ES cells) and, in view of the information provided in the specification, could practice the claimed methods and make and use the claimed compositions without undue experimentation.

In response to the Examiner's statement regarding the "specific nature and composition" of KNOCKOUT™ SR, Applicants note that KNOCKOUT™ SR is the commercial name of a composition described in the specification and used in conjunction with the invention as presently claimed. *See, e.g.*, specification, Tables 1 and 3, pages 27 and 29; *see also* Declaration of Paul J. Price Under 37 C.F.R.§ 1.132 and Declaration of Mary Lynn Tilkins and Under 37 C.F.R.§ 1.132, both submitted herewith. The use of a composition corresponding to KNOCKOUT™ SR for culturing embryonic stem cells is depicted in Examples 1-9 in the specification.

Thus, the references submitted with the June 12 ,2002 Reply (especially Exhibits A, C, D, F and H), in view of the above discussion and the Declarations Under 37 C.F.R. § 1.132, demonstrate that KNOCKOUT™ SR, a composition described in the application and shown to be useful in culturing mouse embryonic stem cells, is also useful in culturing embryonic stem cells from humans and other primates. This evidence therefore provides additional support for Applicants' assertion that the present invention is fully enabled. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Conclusion

Applicants respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Supplemental Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

Claims 127-154 are sought to be added.

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